

HEMATOLOGY COMPONENTS OF THE BLOOD

Whole Blood



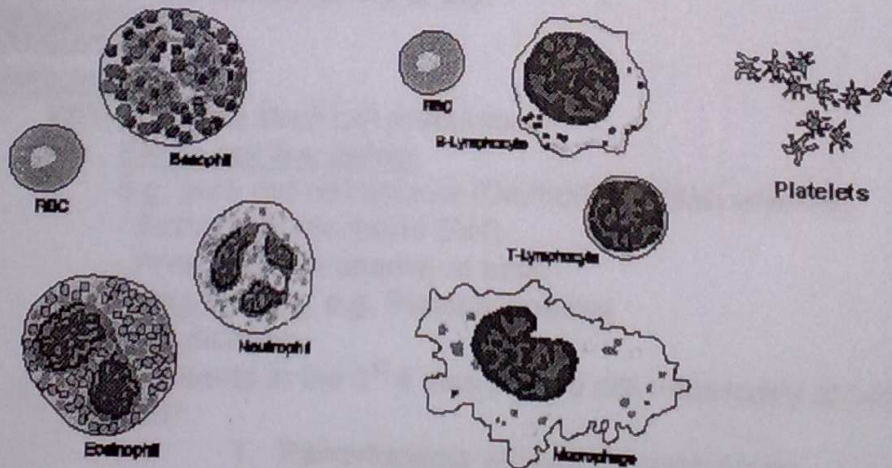
-  Plasma
-  White Blood Cells
6-9000/mm³
-  Platelets
200-400,000/mm³
-  Red Blood Cells
4-5 Million/mm³

Hematocrit (Packed Cell Volume)



- Plasma
- Buffy Coat
(WBC & Platelets)
- RBC's
36%-54%

Blood Cells



Hematology

Anemia

Definition

It is a decrease of Hb % below 11 gm % regardless the age or sex.

Causes

1. Impaired cell synthesis.
2. Hemorrhage.
3. Hemolysis.

Impaired RBCs synthesis

Deficiency of BM Requirement

States originate from decreased intake, increased losses & demand.

1. **Iron deficiency anemia** → Microcytic hypochromic anemia.
2. **B12 & Folic acid deficiency** → Megaloblastic anemia.
3. **B6 deficiency** → Sideroblastic anemia.
4. **Protein deficiency** → Any type of anemia.
5. **Copper deficiency** → Microcytic hypochromic anemia.
6. **Vitamin E deficiency** → Hemolytic anemia.
7. **Vitamin A deficiency** → Microcytic anemia
8. **Vitamin B1** → Hypoplastic anemia.

BM failure

Due to hypoplasia of the BM either 1ry or 2ry.

Primary BM failure

1. Heredofamilial:

With defective stem cell precursors

a. Single cell line defect:

e.g. pure red cell aplasia (Diamond blackfan anemia)
- Autosomal recessive (AR).
- Presents with anemia at birth.

b. Pancytopenia: e.g. Fanconi anemia

- AR disease.
- Presents in the 1st 4 years of life not necessary at birth.
- C/P:

1. Pancytopenia without splenomegaly.

2. Somatic changes:

- Short stature.
- Thumb & radius anomalies.
- Microcephaly.
- Renal defects.

3. Café au lait patches: the skin stains deeply with excess hemosiderin deposition 2ry to ineffective erythropoiesis

- Treatment:

1. BM stimulants: e.g. steroids & anabolics.
2. BM transplantation.

Hematology

II. Idiopathic:

- Mostly due to immunologic process.
- Treatment:
 1. Immunosuppressant.
 2. BM stimulants: e.g. steroids & anabolics.
 3. BM transplantation

Secondary BM failure

- I. Toxins: infection & septicemia.
- II. Drugs: Chloramphenicol, sulfonamides & cytotoxic.
- III. Irradiation:
- IV. Infections: Human parvo virus, Hepatitis B virus & Epstein bar virus.

Dyshemopoietic

1. Infiltration of the BM by malignant or non malignant cells.
2. Try to systemic diseases: endocrinal, hepatic, renal

Iron Deficiency Anemia

Daily requirement of iron: - 2-3 mg / Kg / Day.

EtiologyI. Decrease intake:

1. Infants on cow milk or unfortified artificial milk.....why?.
2. Delayed weaning.why?.

II. Decrease absorption:

1. Chronic diarrhea.
2. Malabsorption syndrome.
3. Excess tea, phytate, oxalate & anti-acids.

III. Excess loss:

Due to chronic blood loss e.g. epistaxis, hemoptysis, hematemesis, ankylostoma, ulcerative colitis & cow milk protein allergy.

IV. Decrease stores:

1. Premature.
2. Low birth weight.

V. Excess requirement:

1. Growing children.
2. Adolescent.

Clinical Picture1. General manifestations of anemia:

- a. Lack of concentration & decrease performance.
- b. Dizziness.
- c. Headache.
- d. Syncopal attack.
- e. Anginal pain.
- f. Muscle cramps & weakness.

2. Red glazed tongue.3. Koilonychia.4. Anorexia & pica.5. Mild splenic enlargement in 10-15 % of cases.

Hematology

Investigations**I. For diagnosis of iron deficiency anemia:**

1. CBC:

- Microcytic hypochromic anemia.
- Low reticulocytic count or even zero.
- No abnormal cells in blood film.

2. Low serum iron ($< 30 \text{ ug / dl}$) & serum ferritin.3. High serum iron binding capacity ($> 350 \text{ ug / dl}$).

4. Increased free erythrocyte protoporphyrin.

II. For diagnosis of the underlying etiology:

1. Stool analysis.....for ankylostoma ova.

2. Occult blood in the stool.

D.D**From other causes of microcytic hypochromic anemia:**

1. Chronic lead poisoning.

2. Thalassemia.

3. Sideroblastic anemia.

Treatment**I. Prophylactic ttt**

1. Adequate iron intake for pregnant females

2. Early & proper weaning.

3. Prophylactic iron supplementation after the 3rd month in premature & low birth weight**II. TTT of the underlying cause**

1. TTT of ankylostoma.

2. TTT of any bleeding focus.

III. Iron therapy**1. Oral :**

a. Liquid ferrous fumarate (45mg) .

b. Tablet ferrous sulfate (60mg) & ferrous gluconate (35mg).

Dose: 6 mg / kg / day elemental iron.

Duration of therapy : 4-6 weeks after correction of anemia.

Side effects: GIT irritation.

Dark stool.

2. Parenteral iron :

a. Fe dextran (100mg).

b. Fe sorbitol (100mg).

The hematological response becomes evident after 48-72 hrs in the form reticulocytosis

VI. Packed RBCs transfusion1. Sever anemia ($\text{Hb} < 6 \text{ gm \%}$).

2. Anemic HF.

3. Surgical emergency.

Megaloblastic anemia

Etiology

It is caused by B12 or folic acid deficiency.

Causes of B12 deficiency

I. Decrease intake:

Very rare as in severe conditions of malnutrition.

II. Decrease intrinsic factor :

1. Partial or total gastrectomy.
2. Pernicious anemia either juvenile or adult type.

III. Consumption of B12 in the intestine:

1. Diphyllbothrium latum.
2. Over-growth of bacteria e.g. in blind loop syndrome.

IV. Decrease absorption:

1. Crohns disease.
2. Resection of the terminal ileum.

V. Decrease stores: Advanced liver disease.



Causes of folic acid deficiency

I. Decrease intake:

Very rare as severe conditions of malnutrition & infants on goat milk.

II. Decrease absorption:

Chronic diarrhea & malabsorption syndrome.

III. Consumption of folic acid due to increase requirement:

Chronic hemolytic anemia.

IV. Drugs:

-Sulfonamides. -Methotrexate.

Clinical picture

1. Manifestations of pancytopenia:

- a. General manifestations of anemia.
- b. Repeated infections.
- c. Bleeding tendency.

2. GIT manifestations :

- a. Recurrent glossitis.
- b. Chronic diarrhea.
- c. Failure to thrive.

3. Neurological manifestations (in B12 deficiency only):

Sub acute combined degeneration of the cord

- a. Peripheral neuritis.
- b. Pyramidal tract affection.
- c. Posterior column affection.

Investigations

I. CBC:

- Macrocytic normochromic anemia.
- Leucopenia (hyper segmented WBCs).
- Thrombocytopenia & Immature platelets.

II. BM aspirate: Megaloblastic changes

III. Serum folate & B12 assay

IV. Schilling test.

V. FIGlu test

VI. Detection of antibodies against the parietal cells of the stomach.

Hematology

Treatment

1. B12 injection 250 mg / 4-8 weeks.
2. Oral folic acid 5 mg / day.

Hemolytic Anemia

Definition

- Anemia due to short life span of RBCs.

Etiology

- Destruction of RBCs due to :
 - A. Corpuscular defect.
 - B. Extra-corpuscular defect.

Corpuscular Defects**I. Acquired:**

Malaria infection.

II. Congenital or hereditary**A. Cell wall defects:**

1. Spherocytosis.
2. Elliptocytosis.
3. Ovalocytosis.

B. Enzymatic defects:

1. Glucose-6-phosphate dehydrogenase deficiency.
2. Pyruvate kinase deficiency.

C. Abnormal Hb:

1. Quantitative defect → thalassemias.
2. Qualitative defect → sickle cell disease.

**Extra-Corpuscular defects****I. Non - immune:**

Infection & DIC.

II. Immune:**A. Iso-immune:**

Rh & ABO-incompatibility

B. Auto-immune:

1. SLE.
2. Idiopathic.

Approach to Diagnosis

Approach to diagnosis should include:

1. The C/P suggesting hemolytic disease.
2. The laboratory finding suggesting hemolytic disease.
3. Determination of the underlying cause by special investigations.

Clinical Picture

According to the C/P, hemolytic anemia is classified into 2 types:

- A. Chronic hemolytic anemia (CHA):** in which hemolysis occurs extra-vascular.
- B. Acute hemolytic anemia (AHA):** in which hemolysis occurs intra-vascular.

Chronic Hemolytic Anemia

Ethnic factors

- Black race → Sickle cell anemia.
- Mediterranean → Thalassemia.

General Clinical picture

- Anemia : not responding to hematinics.
- History of frequent blood transfusion.
- Tinge of jaundice.
- Hepato-splenomegaly: due to:
 - Extra-medullary hemolysis.
 - Extra-medullary hemopoiesis.
 - Hemosiderosis.
 - Intercurrent infection.
- Dark colored stool: due to increased oxidized stercobilinogen.
- Normal colored urine.
- Mongoloid facies : Due to hyperactive BM (in long standing cases).
- Finally can be presented by one of the complications (see later) .
- Positive family history in hereditary causes.

General complications

- Complications of frequent blood transfusion: HBV, HCV & HIV
- Traumatic rupture spleen.
- Hypersplenism.
- Hemosiderosis:
 - Dark colored skin.
 - Cardiomyopathy.
 - HSM.
 - Diabetes mellitus.
 - Peripheral neuropathy.
 - Hypo-endocrinal functions.
 - Leg ulcers.
- Gall stones.
- Heart failure: due to :
 - Anemia.
 - Hemosiderosis.
- Repeated infections: due to :
 - Decrease WBCs if there is :
 - 1) Hypersplenism.
 - 2) Megaloblastic crises.
 - 3) Hypoplastic crises.
 - HF → Repeated chest infection.
 - Decrease tufts in after splenectomy.
- Stunted growth: due to:
 - Anemia → Tissue hypoxia.
 - Hemosiderosis → Hypo-endocrinal functions.
 - Repeated infections.
 - Repeated pathological fracture.

Hematology

- Pathological fracture: due to hyperactive BM.
- Crises:
 - Megaloblastic crises due to folic acid deficiency.
 - Hypoplastic crises → Idiopathic or post viral.
 - Hemolytic crises.
 - Hyper-hemolytic crises if associated with acute hemolytic anemia.

Investigations**I. For diagnosis of chronic hemolytic anemia:****1. CBC:**

- All causes of CHA lead to normocytic normochromic anemia except thalassemia → microcytic hypochromic anemia.
- Increased reticulocytic count
- Abnormal cells can be seen in blood film :
 - Spherocytes → Spherocytosis.
 - Sickle shape → Sickle cell anemia.
 - Target cells & anisocytosis → Thalassemia.

2. Increased serum iron .**3. Low serum iron binding capacity .****4. Increased indirect bilirubin.****5. Stool analysis** → Increased stercobilinogen.**6. Urine analysis** → Increased urobilinogen.**7. Radiological findings:**

- Long bones: - Thin cortex & wide medulla (mosaic pattern).
- Skull :-Wide deploic space (hair on end appearance).

II. For diagnosis of the underlying etiology:**1. Osmotic fragility test** → Spherocytosis.**2. Sickling test** → Sickle cell anemia.**3. Hb-electrophoresis:**

- Increased Hb-F → Beta-thalassemia major.
- Increased Hb-A2 → Beta-thalassemia minor.
- Hb-S → Sickle cell anemia.

4. Alkali denaturation for Hb F in Beta-thalassemia.**5. Acidified serum lyses test (Ham's test)** for paroxysmal nocturnal hemoglobinuria (PNH).

N.B. The diagnostic investigation for hemolytic anemia is decreased red cell survival studies 51 Cr.

Treatment**I. Packed RBCs transfusion:**

1. Ordinary transfusion: Packed RBCs transfusion are given only when Hb% < 6 gm %
2. Hyper - transfusion: Packed RBCs transfusion are given only when Hb% < 10 gm %
3. Super - transfusion: Packed RBCs transfusion are given only when Hb% < 12 gm %

II. Folic acid: 1-5 mg / day.

Pediatrics

Hematology

III. Iron chelating therapy (usually after the age of 5 years):**1. Oral (under trial)****2. Parenteral:**

Desferrioxamine by continuous S.C infusion using portable pump
dose 25 – 40 mg / kg / day.

VI. TTT of complications

Hereditary spherocytosis

Etiology

- Autosomal dominant (AD), in which there is abnormal spectrin in the cell membrane of the RBCs lead to Na influx & water inside the RBCs which lead to deformity of the RBCs , sequestration & destruction in the spleen.
- 10-20 % of cases have no family history.....why?

Clinical Picture

➤ **Age of onset:** can be presented since birth by neonatal jaundice.

- Anemia
- History of frequent blood transfusion.
- Tinge of jaundice.
- Hepato-splenomegaly
- Dark colored stool.
- Normal colored urine.
- Mongoloid facies
- Finally can be presented by one of the complications.

General complications

- Complications of frequent blood transfusion: HBV, HCV & HIV
- Traumatic rupture spleen.
- Hypersplenism.
- Hemosiderosis.
- **Gall stones (common).**
- Heart failure.
- Repeated infections
- Stunted growth.
- Pathological fracture.
- Crises.
- **Complications of neonatal jaundice.**

**Investigations****I. For diagnosis of chronic hemolytic anemia****1. CBC:**

- Normocytic normochromic anemia.
- Increased reticulocytic count
- Blood film : Spherocytes & polychromesla.

2. Increased serum iron .**3. Low serum iron binding capacity .****4. Increased indirect bilirubin.****5. Stool analysis** → Increased stercobilinogen.**6. Urine analysis** → Increased urobilinogen.

Hematology

7. Radiological findings:

- Long bones: - Thin cortex & wide medulla (mosaic pattern).
- Skull: Wide deplcic space (hair on end appearance).

II. Diagnostic investigations

1. Osmotic fragility test : Spherocytes lyses in higher concentration of saline than normal RBCs.
2. Autohemolysis at 24-48 hrs corrected by addition of glucose.

Treatment

1. Packed RBCs transfusion:
2. Folic acid: 1-5 mg / day.
3. Iron chelating therapy usually start after the age of 5 years.
4. TTT of complications:
 - Gall stones : Cholecystectomy.
 - Splenectomy for moderate to severe cases.

Thalassemia

Definition

Quantitative Hb defects

Etiology

Autosomal recessive (AR), in which there is mutation in the globins genes that reduce or totally abolish synthesis of one or more of the globins chains.

1. α -Thalassemia : Reduced or absent α -globins synthesis.
2. β -Thalassemia : Reduced or absent β -globins synthesis.
3. Hereditary persistence of fetal Hb : Synthesis of elevated amount of fetal Hb persists to adult life without causing clinical disease.
4. $\delta \beta$ Thalassemia: both δ and β -globins chains are reduced or absent.

β -Thalassemia

- Genes of β -globins are present on chromosome 11.
- Patients are either heterozygous (β - Thalassemia trait) or homozygous (β - Thalassemia intermedia or β - Thalssemia major).
- β -Thalassemia major differs from β -Thalassemia intermedia being more severe & require more frequent blood transfusion.

Patho-physiology

- Reduced or absent β -globin synthesis prevents adequate Hb accumulation in tetramers. So that cells are hypochromic & microcytic.
- Free α -globin chains, instead accumulate & precipitate during early erythroblast development because α -chains are so insoluble.
- α -Chains are highly toxic to erythroblasts causing intra-medullary hemolysis (ineffective erythropoiesis).
- Some of these cells which pass to the peripheral circulation are deformed cells & have short life span (due to destruction in the spleen).



Hematology

C/P

Age of onset: after the age of 6 months.

- Anemia
- History of frequent blood transfusion.
- Tinge of jaundice.
- Hepato-splenomegaly
- Dark colored stool.
- Normal colored urine.
- Mongoloid facies
- Finally can be presented by one of the complications.

Complications

- Complications of frequent blood transfusion: HBV, HCV & HIV
- Traumatic rupture spleen.
- Hypersplenism.
- Hemosiderosis.
- Gall stones.
- Heart failure.
- Repeated infections
- Pathological fracture.
- Stunted growth.
- Crises.

Investigations**I. For diagnosis of chronic hemolytic anemia:****1. CBC:**

- Microcytic hypochromic anemia.
- Increased reticulocytic count
- Blood film : target cells & anisocytosis.

2. Increased serum iron .**3. Low serum iron binding capacity .****4. Increased indirect bilirubin.****5. Stool analysis** → Increased stercobilinogen.**6. Urine analysis** → Increased urobilinogen.**7. Radiological findings:**

- Long bones: - Thin cortex & wide medulla (mosaic pattern).
- Skull: Wide deploic space (hair on end appearance).

II. Diagnostic investigations:**1. Hb-electrophoresis:**

- Increased Hb-F → Beta-thalassemia major.
- Increased Hb-A2 → Beta-thalassemia minor.

2. Alkaline denaturation test.**III. Anti-natal diagnosis:** By using amniotic fluid or chorionic villous sample.**Treatment****1. Packed RBCs transfusion:****2. Folic acid:** 1-5 mg / day.**3. Iron chelating therapy** usually start after the age of 5 years.**4. TTT of complications:**

1. Gall stones : Cholecystectomy.
2. Splenectomy for hypersplenism.

Hematology

3. Digitalis & diuretics if there's HF.

V. Recent lines of ttt :

1. Neocyte transfusion from single donor.
2. Switch on of the gamma genes by butyrate.
3. Gene therapy.
4. Bone marrow transplantation may provide cure if done early before rise of serum ferritin & liver damage.

 α -Thalassemia

- 4 Genes of α -globin are present on chromosome 16.
- Deletion of one, two, three or four loci result in different types of α -thalassemia.

Types

1. One gene defect $\rightarrow$ Carrier.
2. Two gene defect $\rightarrow$ Mild hemolytic anemia.
3. Three gene defect $\rightarrow$ Hb-H disease (4β) $\rightarrow$ mild to moderate hemolysis.
4. Four gene defect $\rightarrow$ Hb-Barts (4γ) $\rightarrow$ hydrops fetalis.

Sickle cell anemia**Genetics & pathophysiology**

- o Autosomal recessive (AR), results from a point of mutation that changes the amino acid at position 6 on the β globin chain from glutamic acid to valine (Hb-S).
- o Hb-S behaves normally in the oxygenated state, but polymerize on exposure to hypoxia $\rightarrow$ sickling of RBCs.
- o Sick cells are dehydrated, stiff & have shortened life span because they are destructed in the spleen.

Factors that increase sickling :

- a. Low O₂ tension.
- b. Hyperosmolality.
- c. Fever.
- d. Dehydration.

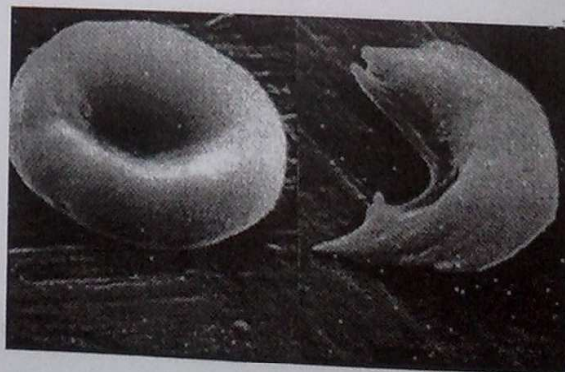
Clinical picture

Age of onset: after the age of 6 months.

Race: Black races are more susceptible.

May present by one of the following crises:

1. Vaso-occlusive crises:
 - Ischemic pain in both hands & foot (Hand foot syndrome).
 - CNS infarction with neurological sequelae.
 - Pulmonary infarction.
 - Splenic infarction (Auto-splenectomy).
 - Sudden blindness.
 - Abdominal angina.
 - Myocardial infarction.
 - Renal infarction.
 - Priapism.



Hematology

2. Hyper hemolytic crises:

- When associated with G-6-PD deficiency.
- Clinically presented with life threatening anemia requiring immediate blood transfusion associated with hemoglobinuria.
- CBC: anemia with high reticulocytic count.

3. Aplastic crises:

- Usually due to infection with parvovirus B19.
- Clinically presented with life threatening anemia requiring immediate blood transfusion.
- CBC: anemia or pancytopenia with low reticulocytic count.

4. Sequestration crises:

- It is due to obstruction of venous return of the spleen → acute massive splenomegaly + shock + collapse.

InvestigationsI. CBC: - Normocytic normochromic anemia.

- Increased reticulocytic count
- Blood film : Sickle shape RBCs.

II. Diagnostic investigations:

1. Sickling test : By addition of the reducing agent (Na-metabisulfite).

2. Hb-electrophoresis: ↑↑↑ Hb-S.

III. Antenatal diagnosis: As thalassemia.**Treatment**I. Vaso-occlusive crises:

- Correction of precipitating factors.
- Adequate hydration.
- Analgesics
- O2 therapy.
- Exchange transfusion is recommended in the management of life threatening conditions as acute chest pain, cerebral strokes or retinal lesions.

II. Sequestration crises:

- Exchange transfusion.
- Urgent splenectomy in severe conditions.

III. Hyper hemolytic crises:

- Blood transfusion.

VI. Aplastic crises:

- Blood transfusion.

V. Additional measures:

1. Folic acid.
2. Routine vaccination against capsulated organisms.
3. Anti-sickling agents:

- Hydroxyurea.
- Erythropoietin.
- Butyrate compound.

4. B.M. transplantation: under trial.

G-6-PD deficiency

Etiology

- X-linked recessive.
- On exposure to oxidizing agents → damage of RBCs.
- Fully expressed in hemizygous male & homozygous female.
- Genetic variants:
 1. Type A⁺ → normal variant in blacks.
 2. Type B⁺ → commonest normal variant.
 3. Type A⁻ → Genetic variant associated with deficiencies in blacks.
 4. Type B⁻ → Mediterranean deficiencies in white races.

Clinical picture

Age of onset: can be presented since birth by neonatal jaundice.

1. History of exposure to oxidizing agents:

- Drugs: Antipyretics except paracetamole, Sulfonamides, Anti-malarial drugs, Chloramphenicol.
- Naphthalene.
- Fava-beans → favism.
- Infections.

2. Sever pallor.

3. Jaundice.

4. Red colored urine due to Hb-uria.

5. Loin pain.

Complications

1. Acute tubular necrosis → acute renal failure.
2. Complications of blood transfusion: HBV, HCV & HIV
3. Anemic heart failure.

Investigations

I. For diagnosis of acute hemolytic anemia:

1. CBC:

- Normocytic normochromic anemia.
- Very high reticulocytic count

2. Increased indirect bilirubin.

3. Decreased haptoglobin & hemopexin.

4. Urine analysis → Hb-uria..

II. Diagnostic investigations:

G-6-PD assay..

Treatment

1. Avoiding of exposure to oxidizing agent.
2. Treatment of infection.
3. Blood transfusion in critically low Hb < 6 gm %.
4. Mannitol or lasix → ↑↑↑ urine flow → prevent tubular necrosis due to Hb-uria.

Bleeding disorders

When to suspect bleeding disorders

- Repeated spontaneous heavy bleeding.
- Bleeding from more than one orifice.
- Prolonged bleeding after minor trauma.
- Petechiae, purpura or ecchymosis.
- Bleeding after circumcision, tooth extraction & repeated hemoarthrosis.

Causes of bleeding disorders

1. Vascular disorders.
2. Platelet disorders:
 - a. Thrombocytopenia.
 - b. Thrombasthenia.
3. Coagulation factors defects either inherited or acquired.

Purpura

Etiology

1. Vascular disorders.
2. Platelet disorders:
 - a. Thrombocytopenia.
 - b. Thrombasthenia.

Vascular disorders

1. Allergic : Henoch-Schonlein purpura (HSP).
2. Vitamin C deficiency.
3. Septicemia: Meningococcal septicemia.
4. Collagen diseases : SLE.
5. Steroid induced or associated with Cushing's syndrome due to defective vascular supportive tissue.

Platelet disorders

I. Thrombocytopenia:

Either due to decreased production or excess destruction.

A. Decreased production:

1. Congenital defects:
 - TAR syndrome.
 - Fanconi anemia.
2. Suppression of BM by:
 - Toxins: infection & septicemia.
 - Drugs: Chloramphenicol, sulfonamides & cytotoxic.
 - Irradiation.

3. Direct invasion of the BM by organisms:

- Human parvo virus.
- Hepatitis B virus.
- Epstein bar virus.

4. Infiltration of the BM by :

- Malignant cells e.g. leukemia or lymphoma.
- Inborn errors of metabolism (IEM).

B. Excess destruction

1. Immune

- ITP.
- Evan \$.
- SLE.
- Transplacental Abs.....neonatal thrombocytopenia.
- Post-transfusion (Antibodies against P- antigen).

2. Non-immune:

- DIC.
- Hemolytic Uremic \$.
- Thrombotic thrombocytopenic purpura.
- Hyper-splenism
- Kasabach Merritt \$ (Giant hemangioma).

II. Thrombasthenia

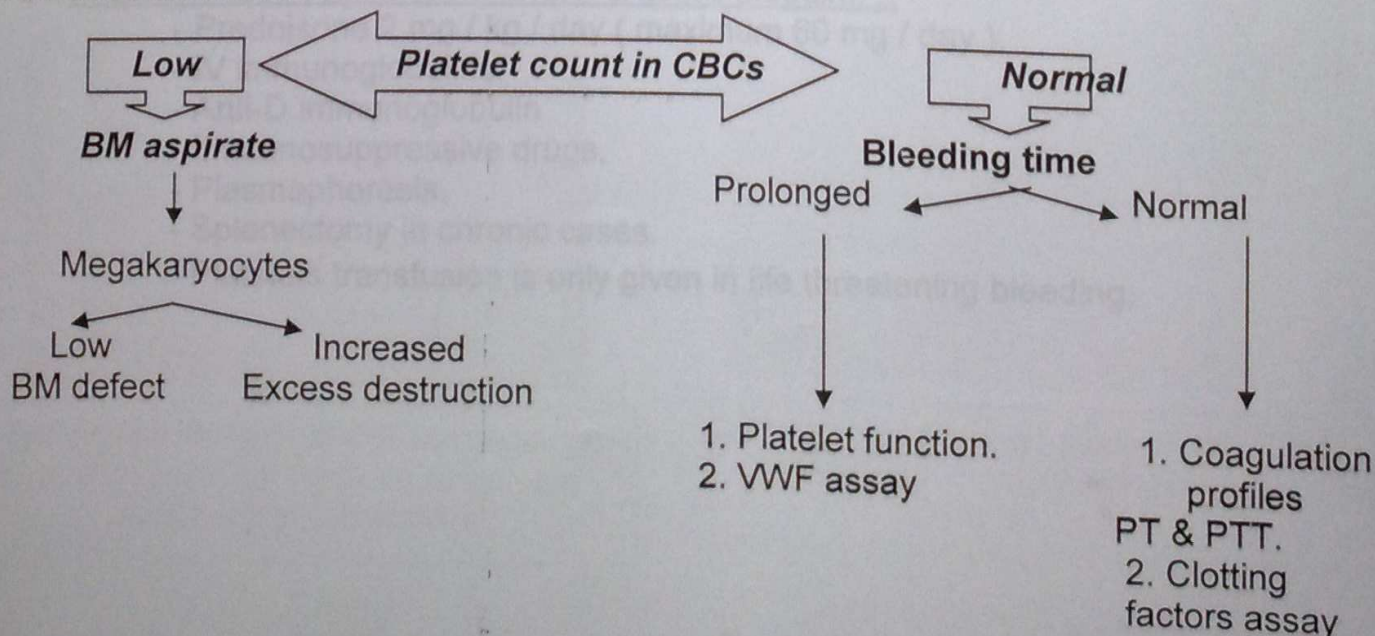
Congenital

1. Von-Willibrand disease.
2. Glanzmann's disease: due to deficiency of glyco-protein IIb & IIIa.
3. Bernard Soulier disease: due to deficiency of glyco-protein Ib (there are thrombocytopenia & thrombasthenia).

Acquired

1. Aspirin & Heparin in high concentration
2. Uremia.

Investigations



Immune thrombocytopenic purpura

Etiology

Auto-immune disease preceded by viral infections as measles, chicken pox, EB-virus or vaccination 1-3 weeks ago.

Clinical picture

1. History of exposure to viral infection 1-3 weeks ago.
2. Skin bleeding: petichae, purpura, ecchymosis or hematoma.
3. Mucus membrane hge.
4. Intra-cranial hge (ICH).
5. No organomegaly, lymphadenopathy or pallor at diagnosis.

Chronic ITP (persistent thrombocytopenia > 1 year)

May be idiopathic or a part of other diseases as SLE, HIV, Hodgkin's disease or Evan syndrome.

The onset is insidious with less severe hge than acute ITP.

The spleen is usually not palpable except with other diseases.

Investigations

1. Bleeding time (BT): ↑↑↑.
2. CBC: ↓↓↓ platelets.
3. Bone marrow aspirate (BM): ↑↑↑ megakaryocytes.

Treatment

I. Acute ITP:

- In mild cases (platelets > 40,000 & no active bleeding): no ttt is given but just follow up.
- In sever cases (platelets < 40,000 & active bleeding):
 - Prednisone 2 mg / kg / day (maximum 60 mg / day).
 - IV immunoglobulins.
 - Anti-D immunoglobulin
 - Immunosuppressive drugs.
 - Plasmapheresis.
 - Splenectomy in chronic cases.
 - Platelets transfusion is only given in life threatening bleeding.

Henoch Schonlein Purpura (Anaphylactoid Purpura)

Etiology

Allergic vasculitis of the small blood vessels in the skin, kidney, joints & GIT.

Clinical picture

1. **Age of onset:** 2-8 years.
2. **Sex :** male : female = 2 : 1.
3. **History of drug intake or upper respiratory tract infection.**
4. **Skin:** palpable purpuric eruptions mostly in the buttocks, extensor surfaces of the legs & forearms.
5. **Kidney:** nephritis → hematuria, oliguria, proteinuria & hypertension.
6. **Joints:** arthritis → red, hot, tender, swollen joints with complete loss of function.
7. **GIT:** Melena & colicky abdominal pain.

Investigations

1. **Bleeding time (BT):** ↑↑↑.
2. **CBC:** normal platelet's count.
3. **Normal platelet's function.**

Treatment

No specific therapy.

1. **Prednisone:** gives symptomatic relief in severe cases & prevent hgic manifestations.
2. **TTT of complications if present :** as intussusceptions & nephritis.



The typical Henoch-Schönlein purpura rash with palpable purpura on an older child's lower extremities



Periorbital edema as commonly seen in young children with Henoch-Schönlein purpura

Hemophilia

Types

1. Hemophilia A (XL-R): due to $\downarrow\downarrow\downarrow$ factor VIIIc.
2. Hemophilia B (Christmas, XL-R): due to $\downarrow\downarrow\downarrow$ factor IX.
3. Hemophilia C (AR): due to $\downarrow\downarrow\downarrow$ factor XI

Hemophilia A

Etiology

- It is XL-R disease ($\downarrow\downarrow\downarrow$ factor VIIIc).
- 33 % have no family history with spontaneous mutations.

Degrees of severity

1. Mild: the level of factor VIIIc is 6-30 % of normal.
2. Moderate: the level of factor VIIIc is 1-5 % of normal.
3. Severe: the level of factor VIIIc is < 1 % of normal.

Clinical picture

1. Neonatal bleeding: bleeding from the umbilicus, after circumcision, after IM injection.
2. Hematoma: usually occurs on minimal trauma.
3. Hemarthrosis.
4. Hematuria.
5. Hemophilic pseudo-tumors: may occur in long bones, pelvis, fingers & toes due to sub-periosteal hges.



Complications

1. Serious life threatening hemorrhage as intracranial hge.
2. Formation of factor VIII inhibitors.
3. Complications of frequent blood transfusions.
4. Joint deformities.
5. Hemophilic pseudo-tumors.

Investigations

1. Bleeding time (BT): normal.
2. Prothrombin time (PT): normal.
3. Partial thromboplastin time (PTT): $\uparrow\uparrow\uparrow$.
4. Factor VIIIc assay.

Treatment

1. Avoid trauma.
2. Replacement therapy:

Product	Factor content	Approximate concentration of FVIII (u/ml)
GFFP	All factors	1
Cryoprecipitate	VIII & fibrinogen	5-10
FVIII concentrates	VIII	20-25

Another preparation to raise factor VIII is Desmopressin DDAVP that stimulates FVIII & vWF release from stores. Dose: 0.3-0.4 ug / kg IVI or intranasal.

3. Antifibrinolytic agent as ϵ -aminocaproic acid & Tranexamic acid to preserve clot.
4. Analgesics as acetaminophen (not aspirin) to control pain.

Von Willibrand disease

- Autosomal dominant disease.
- There is reduced vWF which promotes platelet adhesion & act as a carrier molecule for FVIIIc, protecting it from premature destruction $\Rightarrow$ abnormal platelet adhesion & lower factor VIII activity.

Investigations

1. Bleeding time (BT): $\uparrow\uparrow\uparrow$.
2. CBC: normal.
3. Platelet functions: There is defective platelet aggregation by ristocetin corrected by vWF while aggregation by ADP & collagen is normal.
4. Prothrombin time (PT): normal.
5. Partial thromboplastin time (PTT): $\uparrow\uparrow\uparrow$.
6. Low factor VIIIc & vWF activity.

Treatment

As hemophilia A.

Glanzmann's disease

- o It is due to deficiency of **glycoprotein IIb & IIIa** $\rightarrow$ There is defective platelet aggregation by ADP & collagen while aggregation by ristocetin is normal.

Bernard Soulier syndrome

- o It is due to deficiency of glycoprotein Ib receptors.
- o There is defective platelet aggregation by ristocetin not corrected by vWF while aggregation by ADP & collagen is normal.
- o CBC : Thrombocytopenia & giant platelets.....why?

Vitamin K deficiency

Etiology

1. Inadequate intake.
2. Decreased gut flora : in preterm & prolonged use of broad spectrum antibiotics.
3. Obstructive jaundice $\rightarrow$ $\downarrow\downarrow\downarrow$ absorption.

Liver diseases

All coagulation factors are reduced

Disseminated Intravascular Coagulopathy (DIC)

Definition

- It is wide spread pathological intravascular clotting.

Etiology

1. Endothelial damage: due to hypoxia, acidosis, toxins, burns & irradiation.
2. Hemoconcentration.
3. Slow circulation.

Clinical picture

1. Very bad general condition.
2. Bleeding tendency.....why?.
3. Multi-organ failure.
4. Severe anemia.....why?.

Investigations

1. Bleeding time (BT): ↑↑↑
2. Prothrombin time (PT): ↑↑↑
3. Partial thromboplastin time (PTT): ↑↑↑.
4. CBC: severe anemia & thrombocytopenia.
5. Fibrin degradation products (FDPs): ↑↑↑

Treatment

1. TTT of the causative factors e.g. hypoxia, acidosis, shock, infection & dehydration.
2. Infusion of platelets, FFP, fresh blood.
3. Exchange transfusion especially in the newborn.
4. Fibrinogen IV → in cases of marked hypofibrinogenemia.
5. Heparin 100 U / kg / 4-6 hrs IV → when there is increased thrombosis as in purpura fulminans or hemolytic uremic syndrome.

Purpura fulminans: It is form of DIC in which the clotting phase predominate the picture → Vaso-occlusion → Gangrene of the extremities, nose, lips & ears.

Pancytopenia

Definition

- **Bicytopenia**: decrease in 2 of 3 components.
- **Pancytopenia**: decrease in 3 components

Etiology

1. Aplastic anemia.
2. Megaloblastic anemia either due to B12 or folic acid deficiency.
3. SLE.
4. Paroxysmal nocturnal hemoglobinuria (PNH).
5. Severe infection.
6. Brucellosis.
7. Sarcoidosis.
8. Fanconi anemia.
9. 2ry to bone marrow infiltration:
 - Metastatic cancer.
 - Myelofibrosis.
 - Osteopetrosis.
10. Splenic disorders (Hypersplenism):
 - Lymphoma.
 - Gaucher disease.
 - Nieman-Pick disease.
 - Congestion of the spleen.
 - Kala-Azar.

Clinical picture

1. Manifestations of anemia.
2. Bleeding tendency due to thrombocytopenia.
3. Repeated infection due to leukocytopenia.
4. $\pm$ Splenomegaly.
5. $\pm$ Lymphadenopathy.

Investigations

CBC:

- Pancytopenia.
- Macrocytic anemia....in megaloblastic.
- Reticulocytopenia.....(retics $< 1\%$).
- Reticulocytosis in hypersplenism.
- Thrombocytopenia.
- Neutropenia.

Absolute neutrophil count $< 500 / \text{mm}^3$.

ANC $< 200 / \text{mm}^3$ in very severe disease.

Bone marrow aspirate or biopsy to detect the underlying etiology.

Disorders of leukocytes

Component of the immune system

- B-lymphocytes: responsible for antibodies production.
- T-lymphocytes: responsible for cell mediated immunity.
- Phagocytic system: consists of circulating neutrophils, monocytes & tissue macrophages.
- Complement system acting synergistically with the immune system

Functions of the immune system

1. Prevent & retard local & systemic dissemination of microbial agents.
2. Prevent the development of autoimmune diseases & malignancy.

WBC count

- At birth: 38,000 / ul followed by rapid fall until the end of the 1st week.
- At 1 year: 6,000-17,500 / ul.
- In adult: 4,000-11,000 / ul.

Causes of leukocytosis

1. Physiologic:

- a. Newborn.
- b. Exercise.

2. Acute infections.

3. Acute hemorrhage.

4. Malignancy: leukemia.

5. Hemolytic anemia & after splenectomy.

6. Connective tissue diseases: rheumatic fever & rheumatoid arthritis.

7. Metabolic: DKA & thyrotoxic crises.

8. Drugs: steroid, epinephrine & lithium.

N.B. the increase in WBC count may reach very high level $> 50,000$ / ul this is called leukemoid reaction that has to be differentiated from acute leukemia.

	Leukemoid reaction	Acute leukemia
C/P	Infection	HSM & lymphadenopathy.
Anemia	-ve	+ve
Thrombocytopenia	-ve	+ve
BM aspirate	Normal or hyper cellular	Blast cells

Leucopenia

- Leucopenia is considered when WBC count is $< 4,000 / \text{ul}$.
- It may affect one or more lineages & it is possible to be severely lymphopenic or neutropenic without a reduction in the total WBC count

Neutropenia

- It is considered when PNL count is $< 1,000 / \text{ul}$ in infants between 2 weeks & 1 year, & less than $1,500 / \text{ul}$ beyond that age.

Mechanism

1. **BM & stem cell maturation defect.**
2. **Suppression of neutrophil production:**
 - a. Severe infection.
 - b. Malignant deposit in the BM.
 - c. Drugs: sulfonamides & anti-convulsions.
3. **Increased destruction of neutrophils:** Immune mediated: neonatal immune neutropenia & SLE.

Clinical picture

Severe neutropenia ($< 500 / \text{ul}$) has common clinical manifestations

1. High fever & toxemia.
2. Extensive oral ulcers.
3. Gram -ve septicemia.

Laboratory findings

1. **CBC:** neutropenia.
2. **BM:** marked reduction of myeloid series or maturation arrest.
3. **Measurement of neutrophil antibodies.**
4. **Serologic tests for SLE.**
5. **BM culture for stem cells.**

Treatment

1. Proper antibiotic therapy for eradication of infections.
2. Proper ttt of the underlying cause.

Esinophils

- They are produced & mature inside the BM $\Rightarrow$ migrate to tissue sites (epithelium of intestine specially the colon).
- The ratio of blood to tissue esinophils is about 1 : 100 .
- In response to allergen or tissue parasites $\Rightarrow$ migrate to tissues (lung in BA, or intestinal wall following parasitic infestation.

Causes of esinophilia ($> 400 / \text{ul}$)

1. **Allergy:** BA, hay fever & eczema.
2. **Parasitic infestations**
3. **Others:** Hodgkin's, polyarteritis nodosa, Addison disease.

Causes of esinopenia

1. Cushing disease.
2. Steroid therapy.

Lymphocytes

Causes of lymphocytosis

1. **Physiologic**: between 4 months & 4 years

2. **Infections**:

Acute:

- a. Moderate in measles, rubella, mumps, typhoid fever.
- b. Marked in IMN, CMV, Toxoplasmosis & pertussis.

Chronic: TB.

3. **Acute lymphoblastic leukemia.**

Causes of lymphopenia

1. **Congenital B-cell deficiency** $\Rightarrow$ deficiency of immunoglobulins $\Rightarrow$ recurrent bacterial infections

2. **Congenital T-cell defect**: it is more severe than B-cell defect $\Rightarrow$ impaired cell mediated immunity $\Rightarrow$ repeated viral infections, TB, GVHD.

Leukemia

It is the most common form of childhood cancer.

Acute leukemia constitute 97 % of all childhood leukemia & consist of two types:

- Acute lymphoblastic leukemia (ALL) : 80 %.
- Acute non-lymphoblastic leukemia (ANLL) : 20 %.

Chronic leukemia constitute 3 % of childhood leukemia & consists of 2 types:

- Adult type of chronic myeloid leukemia (Philadelphia chromosome +ve).
- Juvenile type of chronic myeloid leukemia (Philadelphia chromosome -ve).

Incidence

1. 1 : 25,000 population.
2. Peak incidence: 2-5 years.
3. Account for 25-30 % of all childhood cancers.

Etiology

Unknown, but the following factors have been condemned:

1. **Ionizing radiations**.
2. **Chemicals** (benzene in ANLL).
3. **Drugs** (alkylating agents).
4. **Genetic considerations** because there is increase incidence in:
 - Identical twins.
 - In siblings.
 - With chromosomal abnormalities.
 - In genetically determined diseases as ataxia telangiectasia & agammaglobulinemia.

Clinical picture

1. General systemic effects:

- Fever.
- Anorexia.
- Loss of weight.

2. Hematologic effects due to BM invasion:

- Anemia → pallor, easy fatigability, dyspnea & tachypnea.
- Neutropenia → fever, ulceration of buccal mucosa & repeated infections.
- Thrombocytopenia → petichae, purpura

3. Manifestations from lymphoid system invasion:

- Lymphadenopathy.
- Hepatosplenomegaly.

4. CNS invasion:

↑↑↑ Intracranial tension (severe headache in the early morning, vomiting, blurring of vision, bilateral VI cranial nerve palsy & papilledema).

- Parenchyma involvement : hemi paresis, cranial nerve palsies & convulsions.
- Hypothalamic manifestations.
- Cerebellar manifestations.
- Intracranial hges.

5. Genitourinary tract involvement:

- Testicular enlargement.
- Renal involvement: hematuria, hypertension & renal failure.

Hematology

6. Gastro-intestinal involvement:

- Bleeding.
- Abdominal mass.
- Peritonitis & septic shock.

7. Bone & joint involvement:

- Generalized bone aches.
- Multiple osteolytic bone lesions.

8. Skin involvement:

- Skin masses can be presented especially in neonatal or ANLL.

9. Cardiac involvement: leukemic infiltration of the heart is very rare.**10. Lung involvement:** by blast cells.**Investigations****1.CBC:**

- Hb % : moderate to marked reduction.
- WBCs : low, normal or increased.
- Platelet's count: ↓↓↓.
- Blood film: Blast cells.

2.Bone marrow aspirate: diagnostic .**3.CXR:** - Mediastinal mass (T-cell leukemia).
- Lung infiltrates.**4.Skeletal survey:** transverse metaphyseal lines.**5.Blood chemistry:**

- Serum electrolytes.
- Renal functions.
- Serum uric acid.
- Liver functions.

6.CSF examination.**7.Coagulation profile:** decreased coagulation factors in ANLL.**8.Cardiac function:** ECG & echo-cardiography.**Risk factors in leukemia:**

Depends on several factors including:

- Age: < 1 years & > 10 years.
- Sex: males.
- Organomegaly: huge spleen.
- CXR: Mediastinal shadow (T-cell leukemia).
- CNS involvement.
- Testicular involvement.
- Blast cells at diagnosis > 20,000 / mm³.
- Platelet's count at diagnosis < 100,000 /mm³.
- Hb % at diagnosis > 10 gm %.
- Morphologic, cytogenetic & molecular characteristics

Treatment**General care**

**** Supportive psychological care.**

**** Supportive medical care:**

- Packed RBCs.
- Platelets transfusion.
- Good hydration.
- Alkalinization of urine.
- Allopurinol 10 mg / kg / day.
- Broad spectrum antibiotics for eradication of infections.
- Live attenuated vaccines is contraindicated.
- Growth factors to correct neutropenia.

Specific therapy

- To induce clinical & hematological remission.
- To maintain remission.
- Prevention of CNS infiltration.
- Ttt of complications.

Therapy includes:

- Systemic chemotherapy.
- Intra-theal chemotherapy as CNS prophylaxis.
- Radiotherapy.
- BM transplantation.

Assessment of remission :

- No symptoms or signs related to leukemia.
- Normal CBC.
- BM aspirate: < 5 % blasts.

Causes of death

- Organ failure.
- CNS infiltration & hges.
- Secondary malignancies.

Lymphomas

The 3rd most common tumor of childhood, after leukemia & brain tumors.

Types

1. Hodgkin's.
2. Non-Hodgkin's.

Hodgkin's Lymphoma

- **Age:** Rare < 5 years.
Peak incidence is at 13-35 years.

- **Sex:** Male : Female ratio = 2 : 1.

Clinical staging

Stage I :

Only one group of LNs....Or..... One extra-lymphatic site.

Stage II :

More than one group of LNs ± localized extra-lymphatic site
All should be at the same side of the diaphragm.

Stage III :

As stage II ,but on both sides of the diaphragm ± spleen.

Stage IV :

Diffuse or disseminated involvement of one
or more extra-lymphatic organs ± associated LN enlargement.

Each stage is further divided into A or B.

A → no systemic symptoms.

B → Systemic symptoms as fever, night sweats & weight loss.

Clinical picture

1. **Painless swelling** of one or more superficial LN (firm, rubbery, not tender, discrete, single or multiple, with no regional inflammation).
2. **Mediastinal** \$ if mediastinal LNs are affected:
 - Persistent non-productive cough.
 - Congested non pulsating neck veins.
 - Hoarseness of voice.
 - Dysphagia in sever conditions.
3. **Constitutional symptoms** : Loss of weight, intermittent fever, anorexia & easy fatigability.
4. **Manifestations of extra-nodal involvement.**

Investigations

1. LN biopsy is diagnostic by identification of Reed-Sternberg cells in tumor tissues.

According to histo-pathology it is classified into 4 types :

- Lymphocyte predominant type (10-20 %) : Best prognosis.
- Nodular sclerosing type (50 %) : Favorable prognosis.
- Mixed cellularity type (40 %) : Less favorable prognosis.
- Lymphocyte depletion type (< 10 %) : Very bad prognosis.

Hematology

2. Other investigations as CXR, pelvi-abdominal U/S, CSF & BM aspirate are needed for staging of the tumor.

Treatment1. Conservative ttt:

- Packed RBCs for correction of anemia.
- Platelet concentrate for correction of thrombocytopenia.
- Broad spectrum antibiotics for eradication of infections.

2. Chemotherapy:3. Radiotherapy.**Non-Hodgkin's Lymphoma**

- It is more common than Hodgkin's lymphoma in young children. It is predisposed by immunodeficiency (congenital or acquired).
- EBV is the cause of African type of Burkett's lymphoma

Staging

Stage I: Single mass or LN (not in the mediastinum or the abdomen).

Stage II: Two masses on the same side of the diaphragm.
Or small 1ry GIT tumor $\pm$ mesenteric LN only.

Stage III: Two single tumors on both sides of the diaphragm.
Or any 1ry intra-thoracic.
Or extensive intra-abdominal disease.

Stage IV: CNS or BM infiltration.

Clinical picture

1. Painless unexplained swelling of cervical or supra-clavicular LN.

2. Rapidly growing tumor.

3. Other clinical manifestations are variable depends on the site of the 1ry tumor & extent of local & distant spread.

Investigations

As Hodgkin's lymphoma but pathologically it is classified into small & large cell types.

Treatment

As Hodgkin's lymphoma but with different protocol of chemotherapy.
CNS prophylaxis is essential for T-cell & Burkett's type

Burkett's LymphomaAfrican type:

- Affects children previously infected with EBV.
- It involves bones of the face as maxilla & orbit.
- It is **very sensitive** to irradiation & chemotherapy, but has high tendency to relapse.

American type:

- Affects young adults.
- Not associated with EBV.
- Usually of abdominal origin.
- Higher BM & CNS involvement.

Lymphadenopathy

Etiology

A. Non-specific reactive hyperplasia.

1. Infections:

• Viral:

- Infectious mononucleosis.
- Cytomegalovirus.
- Rubella & rubeola.
- Varicella.
- Herpes simplex.

• Bacterial:

- TB.
- Brucella.
- Salmonella.
- Staph & streptococcus.

• Protozoa: e.g. toxoplasmosis.

• Spirochete: e.g. syphilis.

• Fungal: e.g. coccidiomycosis.

2. Connective tissue disorders:

- o Rheumatoid arthritis.
- o SLE.
- o Kawasaki disease

3. Hypersensitivity states:

- o Serum sickness.
- o Drug reaction e.g. INH, antithyroid.



B. Lymphoproliferative disorders

1. Neoplastic disorders:

- o Hodgkin & non- Hodgkin's lymphoma.
- o Leukemia.
- o Metastases.
- o Histiocytosis.

2. Storage diseases:

- o Nieman-Pick disease.
- o Cystinosis.

3. Granulomatous diseases:

- o Sarcoidosis.
- o Chronic granulomatous disease.

4. Miscellaneous:

- o Hyperthyroidism
- o Post-vaccination

Pediatrics

Hematology

Management

History

- Duration of lymphadenopathy.
- History of infection.
- History of systemic complaint e.g. Wt loss, night sweating, arthritis or arthralgia, generalized bone aches

Examination

- **General examination** for evidence of hematological disease e.g. pallor, purpura & hepatosplenomegaly.
- **Lymph node examination:**
 1. **Site:**
 - Enlarged tonsillar or inguinal LNs is most likely due to localized infection.
 - Enlarged supraclavicular & axillary's LNs are most likely to be of a serious nature.
 2. **Size:**
 - LN > 2.5 cm & that increase in size should be considered pathologic.
 3. **Number:**
 - Is it localized or generalized.
 - Or start localized then become generalized.
 4. **Consistency:**
 - Malignant LNs are usually firm or rubbery.
 - Fluctuant & warm LNs usually associated with infections.
 5. **Tender or not**
 - Tender LNs usually associated with infections
 - Malignant LNs are usually not tender.
 6. **Relation to each others:**
 - tuberculous LNs usually matted together.
 7. **Relation to underlying structures:**
 - If LNs are attached to underlying structures usually malignant
 8. **Relation to overlying skin:**
 - Tuberculous LNs may be attached to overlying skin & may be associated with ulcer.

Investigations

- **CBC & ESR.**
- **Skin test:** for TB & Fungal infection.
- **Bacteriological culture:** for regional lesion.
- **Serologic test** for Toxoplasmosis, CMV & EBV.
- **Radiological investigations:** CXR, Abdominal sonar & CT if indicated.
- **Bone marrow aspiration or biopsy** may be needed if hematological disease is suspected.
- **LN biopsy if:**
 - a. Malignancy is suspected.
 - b. Laboratory investigations is not conclusive.
 - c. Size > 2.5 cm.
 - d. Persistent LN or has progressive course.
 - e. Not responding to antibiotics for 1 month.

Splenomegaly

- The tip of the spleen is frequently palpable in normal infants & young children up to 3-4 years of age. At older age, a palpable spleen usually indicates splenic enlargement.
- Palpable spleen may be due to visceroptosis rather than splenomegaly.

Etiology

A. Infections.

Acute

- Viral:
 - Infectious mononucleosis (IMN).
 - Cytomegalovirus (CMV).
- Bacterial:
 - Subacute bacterial endocarditis (SBE).
 - Salmonella (typhoid fever).
- Protozoa: e.g. malaria
- Rickettsial.

Chronic:

- Bacterial:
 - Subacute bacterial endocarditis (SBE).
 - TB.
 - Brucellosis.
- Spirochete: e.g. syphilis
- Protozoal: e.g. malaria, toxoplasmosis & Schistosomiasis.
- Fungal: e.g. coccidiomycosis

B. Hematological disorders

1. Hemolytic anemia:

- Thalassemia.
- Spherocytosis.
- Splenic sequestration in sickle cell ane

2. Extramedullary hematopoiesis as:

- Myelofibrosis.
- Osteopetrosis.

3. Myeloproliferative disorders: e.g. polycythe

C. Infiltrative disorders

1. Non- malignant :

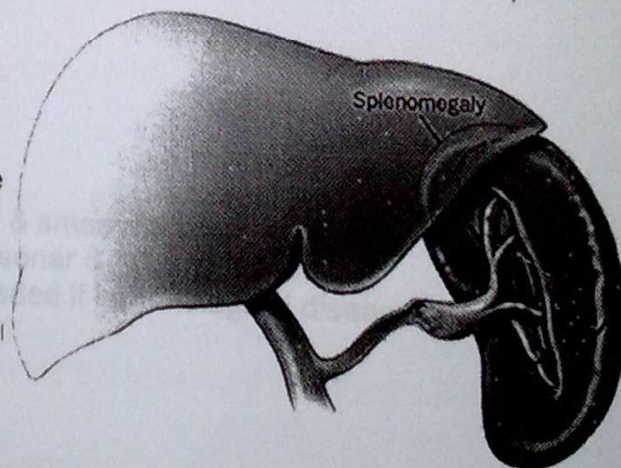
- Histiocytosis.
- Storage disease:
 - Gaucher's disease.
 - Niemann-Pick.
 - Mucopolysaccharoidosis.

2. Malignant as:

- Leukemia.
- Lymphoma.

D. Congestive splenomegaly

- All causes of portal hypertension.....see notebook of GIT.



Hematology

E. Hypersensitivity states

- Serum sickness.
- Connective tissue disorders:
 - Rheumatoid arthritis.
 - SLE.

F. Primary splenic disorders

- Cysts.
- Benign tumors (hemangioma).
- Hemorrhage in the spleen (e.g. subcapsular hematoma).

Management**History**

- Fever & rigors → infection.
- History of neonatal umbilical sepsis → portal vein thrombosis.
- History of jaundice → liver disease.
- Generalized bone aches & bleeding tendency → leukemia.
- +Ve family history of CHA.
- History of trauma → subcapsular hematoma of the spleen.

Examination

- Size of spleen, consistency, tenderness.
- Hepatomegaly.
- Lymphadenopathy.
- Fever.
- Purpura.
- Jaundice.
- Manifestations of rheumatoid arthritis & SLE.
- Splinter hge.
- Cardiac murmur.

Investigations

- CBC & ESR.
- Skin test: for TB & Fungal infection.
- Bacteriological culture: for regional lesion.
- Serologic test for Toxoplasmosis, CMV , EBV & smear for malaria.
- Radiological investigations: CXR, Abdominal sonar & CT if indicated.
- Bone marrow aspiration or biopsy may be needed if hematological disease is suspected.
- Liver function tests.
- Investigations of portal hypertension.
- Enzymatic assay for Gaucher.
- C3, C4 & ANA If connective tissue diseases is suspected.
- LN biopsy if significant lymphadenopathy:
- Biopsy: Partial biopsy & splenic aspiration are rarely performed because there is a significant risk of bleeding.

DIFFERENTIAL DIAGNOSIS OF ABDOMINAL MASSES IN INFANTS AND CHILDREN

I-GENITOURINARY DISORDERS

A. Renal disease

- Mass in the loin except in kidney malformations. Associated findings may be abdominal pain and tenderness, hematuria, hypertension, evidence of urinary tract infections, deterioration of renal functions
- Causes
 1. Hydronephrosis
 2. Polycystic kidney.
 3. Solitary renal cysts
 4. Renal vein thrombosis
 5. Ectopic or horse-shoe kidney
 6. Perinephric abscess

B- Bladder distension

- Mass is globular, in middle line, usually below umbilicus
- Causes
 1. Posterior urethral valve (more in neonates)
 2. Anticholinergic drugs
 3. Spinal cord lesions: tumors, trauma, congenital abnormalities
 4. Infection of bladder, urethra, or pelvis

C-Urachal Cyst

Palpated as middle line cystic swelling below the umbilicus, attached to the abdominal wall

D-Uterine enlargement

Hydrometrocolpos (prepubertal) and Hematocolpos (post-pubertal): Due to imperforate hymen, distension of the uterus by accumulated secretions and menses. Palpated as pelviabdominal mass

E-Ovarian disorders

Ovarian cysts and tumors are uncommon in childhood

II- NEOPLASMS

A-Wilms' tumor

*Wilm's tumor is a mixed neoplasm composed of metanephric blastema with stromal and epithelial derivatives at various stages of differentiation.

*The most common features at presentation are:

- Abdominal mass - in 80% of patients, the mass is lateral and nodular and may be visible on inspection
- Abdominal pain in 30% of patients - usually vague and poorly defined
- Haematuria in 25% of patients, usually microscopic

*Metastases are present in 20%. They mostly affect the liver and lungs, and occasionally, bone.

*General symptoms are commonly anorexia, weight loss, fever and anaemia.

*There may be hypertension or erythrocytosis.

B-Neuroblastoma

*A tumor derived from neural crest tissue the most common sites are:

- 50% adrenal medulla
- 25% abdominal sympathetic ganglia

*Clinical features:

Depend upon the site of the primary tumor and the extent of metastases; the symptoms can be very varied. Half of cases present with advanced disease. Local infiltration, lymphatic spread, and haematogenous spread, particularly to liver, lungs and bone, is common.

*General effects of malignancy: pallor - anemia - fever, weight loss, anorexia, irritability, and failure to thrive

*Local tumor effects:

- An abdominal mass is common - it may cross the midline and be difficult to distinguish from the liver
- Local invasion may cause the cauda equina syndrome, or paraplegia

*Metastatic spread: proptosis, Horner's syndrome, dysphagia, lung collapse, bone pain and pathological fracture, periorbital bruising looking like a black eye is seen in children, skin nodules

*Increased catecholamines secretion: flushing, cerebellar ataxia, diarrhoea, hypertension is rare

C-Lymphoma

Enlargement of the liver and spleen are common, but abdominal lymph nodes are frequently enlarged

D-Teratoma

Abdominal. mass high in the retroperitoneal region, usually in first two years of life .X-ray show spotty calcification

E-Mesoblastic nephroma

Rare embryonic tumor, usually presents at birth

F-Rhabdomyosarcoma

Rare, highly malignant tumor that originates from striated muscle.

III- **INTESTINAL DISORDERS**

A-Fecal material

In constipation ,masses of impacted stools are palpable in the left lower quadrant mobile, disappear after enema

B-Intussusception

Other symptoms such as pain and vomiting are prominent than the mass that is felt in right lower or upper quadrant

Hematology

C-Intestinal duplication

In addition to the mass, abdominal pain, vomiting, and GIT hemorrhage may be present

D-Malrotation with volvulus

The sudden onset of pain and vomiting herald this serious event

E-Bezoar

In premature infants fed milk with high casein content may develop lactozoars. Hair ingestion may also result in gastric masses

F-Intestinal tumors

Lymphomas, leiomyosarcomas and other tumours are uncommon

G-Inflammatory lesions:

1. Tabes mesenterica
2. Appendicular mass : inflamed appendix with an adherent covering of omentum and small bowel. The history is similar to that of appendicitis with a longer duration since onset. Examination reveals a mass in the right iliac fossa.
3. Abscess

H-Pyloric stenosis

Occurs in neonates and first months of life ; characteristic "projectile" vomiting .Examination reveals the distended stomach and a smooth ovoid mass just below the right costal margin, which is the hypertrophied pylorus.

IV -BILIARY DISORDERS

A-Choledochal cyst

Mass in right upper quadrant with jaundice and pain

B-Hydrops of gall bladder

Infants with acute hydrops present with poorly localized continuous abdominal pain and mass in right upper quadrant

C-Distended gall bladder

Occasionally occurs in cystic fibrosis

V-MISCELLANEOUS CAUSES

A-Pancreatic cyst

Following blunt trauma to the abdomen, mass in epigastrium or upper left quadrant with or without ascites

B-Abscesses

Abdominal abscesses are frequently associated with fever, abdominal discomfort or pain, anorexia, +/- vomiting and diarrhea

C-Adrenal hemorrhage

More in neonates, felt as loin mass

D-Aortic aneurysm

Rare, mass is pulsatile

BLOOD AND BLOOD COMPONENT TRANSFUSION

Differentiation should depend on

- History and physical examination
- Investigations should include CBC, ESR, liver and renal functions , abdominal sonar, CT abdomen and MRI if needed
- Other specific investigations may include IVP, isotopic scan
- Assessment of urinary catecholamines if suspect neuroblastoma

THE AGE OF THE AFFECTED CHILD IS IMPORTANT:

Neonates	Early childhood	Adolescents
- Hydronephrosis an/or enlarged bladder (PKD, PUV, UPJ obstruction)	- Tumours ~Wilms',	- Fecal material
- Renal vein thrombosis	- neuroblastoma,	- IBD
- Hepatoma/hemangioma	- rhabdomyosarcoma, non-	- Abscess
- Storage disease	- Hodgkin's lymphoma,	- Tumours
- Choledochal cyst	- hepatic, ovarian)	- Ovarian cyst/torsion
- Duplication	- Pyloric stenosis (3-6 wk)	- Pancreatic
- Ovarian cyst	- Intussusception (3-6 mo)	- pseudocyst
- Teratomas	- Duplication cysts	- Choledochal cyst
- Hydrocolpos/hematocolpos	- Mesenteric cysts	- Bladder distension
- Adrenal hemorrhage	- Hydronephrosis	- Hydrometrocolpos
- Mesenteric/omental cyst	- Renal malformation	
Mesoblastic nephroma	- Fecal material	
- Volvulus	- Choledochal cyst	
- Other congenital lesions	- Bladder distension	
	- Pancreatic pseudocyst	
	- Other congenital lesions	

BLOOD AND BLOOD COMPONENT TRANSFUSION

Facts about blood:

- Blood is composed of plasma, water and cellular components (red blood cell, white blood cells and platelets)
- Blood and blood products are used to treat accident and burn victims, cancer patients and other patients undergoing surgeries and medical treatments.
- Red blood cells can be stored for up to 42 days
- Platelets can be stored for only five days
- Frozen plasma can be stored for as long as one year
- Persons belonging to the 0 -ve blood group are called universal blood donors. The RBCs of a universal blood donor may be transfused to anyone regardless of their blood type.
- The plasma of those belonging to the AB blood group may be transfused to anyone regardless to their blood type.
- More than 90% of transfusion complications have been attributed to the presence of leucocytes in allogeneic blood.
- The maximum allowable time for the transfusion is four hours.
- The transfusion rate should be determined by the patient clinical status.
- Because blood donations often are separated into several components (RBCs, plasma, platelets, for instance).
- One donation can help save three lives.

Red Blood cell transfusion

They are the most frequently transfused blood component.

Indications:

- 1- Acute hemorrhage: blood loss > 25% of the circulating blood volume.
- 2- Symptomatic anemia (hemoglobin < 7-8 gm / dl) and patients with chronic anemia secondary to bone marrow suppression.
 - The decision to transfuse RBC should be based only on blood hemoglobin levels because children with chronic anemia may be asymptomatic despite low hemoglobin level
 - Factors considered in the decision to transfuse RBCs other than Hb level are: 1) Patient's symptoms and signs, 2) Cause of anemia, 3) Alternative therapies e.g. recombinant human erythropoietin (EPO) therapy which has reduced the need for RBC transfusion in certain diseases e.g. chronic renal insufficiency.
 - RBCs transfusion for thalassemia and sickle cell anemia (see chapter ...). The dose recommended for pediatric population is 10-15 mL / Kg. The patients with active bleeding or hypersplenism might require additional RBC

transfusion to maintain or increase their hemoglobin.

In chronic RBCs transfusion:

- Cross matching should be performed before each transfusion to decrease the alloimmunization and transfusion reaction.
- Packed RBCs should be relatively fresh
- Leukoreduction should be used (see below).
- Transfused blood should be screened and the patient should be vaccinated.

Neutrophil (Granulocyte) transfusions

- Infected neutropenic patients usually respond to antibiotics alone provided bone marrow recovers early in infection.
- Newly diagnosed leukemia respond to induction chemotherapy, they do not need granulocyte transfusion. In contrast, infected children with sustained bone marrow failure and severely neutropenic ($< 0.5 \times 10^9/L$) may benefit when granulocyte transfusion are added to antibiotics.
- Children with qualitative neutrophil defects may need granulocyte transfusion added to the antibiotics when presenting with progressive life threatening infection.

These disorders are chronic and because of the risk of alloimmunization granulocyte transfusion are recommended only when infection are clearly unresponsive to antimicrobial drugs.

Platelet transfusions

- Platelets can be obtained from a unit of whole blood or collected by apheresis.
- The volume, platelet content and dose of platelets will depend on the method of collection used.
- The storage time is 5 days (once pooled the storage time becomes 4 hours).

Indications for platelet transfusion:

- Treatment of bleeding or its prevention prior to an invasive procedure in patients with platelet count $< 50 \times 10^9/L$.
- Bleeding prophylaxis in patients with platelet count $< 10 \times 10^9/L$ secondary to bone marrow suppression.
- In patients with congenital or acquired platelet dysfunction, platelet transfusion are justified only if significant bleeding occurs. Because PLT dysfunction may be present long time and repeated transfusion may lead to alloimmunization and refractoriness. In these patients, alternative therapies, particularly desmopressin acetate should be considered to avoid PLT transfusions.
- In the absence of life threatening bleeding, platelet transfusion may be

contraindicated in idiopathic thrombocytopenic purpura and thrombotic thrombocytopenic purpura.

Plasma transfusion

- Plasma is obtained from a unit of whole blood and contains approximately 200-220 ml/bag. *Plasma dose is 15 ml / Kg.*
- It is stored frozen for up to one year.
- Transfusion of fresh frozen plasma (FFP) is used in the treatment of bleeding or prior to an invasive procedure in patients with acquired or congenital coagulation factor deficiencies (II, V, VII, X).
- Factor XIII and fibrinogen deficiencies are treated with cryoprecipitate.
- Transfusion of FFP or cryoprecipitate is no longer recommended for treatment of patients with severe hemophilia A or B, because safer factor VIII and IX concentrates are available. Moreover, mild to moderate hemophilia A and certain types of von Willebrand's disease can be treated by DDAVP.
- The use of plasma is also indicated for fluid replacement during plasma exchange in patients with thrombotic thrombocytopenic purpura.
- FFP is used for rapid reversal of warfarin effects in patients who are actively bleeding.
- FFP contains several anticoagulant proteins (antithrombin III, protein C and protein S) whose deficiencies have been associated with thrombosis. FFP may be used as a replacement therapy in these patients.

Cryoprecipitate

- Cryoprecipitate is prepared from a unit of FFP
- Cryoprecipitate contains only fibrinogen and factors VIII and XIII
- Transfusion of cryoprecipitate is indicated for treatment of bleeding or its prevention prior to an invasive procedure in patients with hypofibrinogenemia.
- Cryoprecipitate is also used in the preparation of fibrin glue which is a topical adhesive used for certain surgical procedures and consists of a mixture of thrombin and cryoprecipitate.

Risks of blood transfusion

I) Infectious risks:

transmission of:

- HIV
- Hepatitis B & C
- CMV (can be eliminated by transfusing cellular blood products filtered with leucocyte filters)
- Syphilis
- Parvovirus B19

- Epstein-Barr virus
- Chagas disease

II) Risks of non-infectious nature

- Febrile transfusion reaction
- Fluid overload
- Graft versus host disease
- Electrolytes and acid base imbalances
- Iron overload
- Increased susceptibility to oxidant damage
- Exposure to plasticizers
- Hemolytic transfusion reaction (immediate or delayed)
- Immunosuppression and alloimmunization.

N.B.

Patients known to have immune dysfunction are at increased risk of post transfusion graft versus host disease. For these patients all cellular blood components should be irradiated before transfusion, but frozen acellular products such as FFP do not require it.

Leukoreduction

What is leukoreduction?

It is a process of removing > 99.9% of WBCs from cellular blood components (red cells and platelets).

Method for leukoreduction:

Almost all red cells are leukoreduced using a specific filter. Washing was used as a method for leukoreduction but is not very efficient resulting in only 90% WBCs removal.

Indications:

- 1- Recurrent fever chill reactions.
- 2- Immediate or delay alloimmunization to HLA antigens
- 3- The risk of CMV transmission.